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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,479	11/22/2000	Doris Coit	PP01617.002	2173

7590 02/25/2002

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EXAMINER
BROWN, STACY S

ART UNIT	PAPER NUMBER
1648	21

DATE MAILED: 02/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/721,479	Applicant(s) COIT ET AL.	
	Examiner Stacy S Brown	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *20-31 and 33-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 November 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of Group I, claims 1-19 and 32 is acknowledged and entered. Claims 1-42 are pending. Claims 20-31 and 33-42 are withdrawn from consideration being drawn to non-elected inventions. Claims 1-19 and 32 are examined on the merits.

Election/Restrictions

2. Applicant's traversal of the restriction requirement has been carefully considered, but not found persuasive. Applicant mainly traverses that no burden of search has been established between Groups I and II, Groups III and VI, and Groups V and VI. Applicants assert that because of their similar classification and dependency from claim 1, there is no burden to the examiner to search all claims, or at least the claims of one of Groups I and II, Groups III and VI, and Groups V and VI. Contrary to Applicant's assertions, the polypeptides and polynucleotides of inventions I and II constitute a burdensome search because they require separate amino acid and nucleic acid sequence searches; further, they are chemically distinct products, not disclosed as capable of use together. The methods of invention III and VI are unrelated, having different method steps, functions, outcomes and effects, and are not disclosed as capable of use together. The method of preparing a polypeptide and the method of eliciting an immune response are not disclosed as capable of use together and have different modes of operation, function and effect. Therefore a search of both methods would be burdensome. Inventions V and VI, drawn to methods of eliciting an immune response by administering a polypeptide or polynucleotide, are unrelated. Methods of administering a polypeptide and methods of administering polynucleotides (gene therapy) comprise different materials, modes of operation, function and effect. A search of administering a polypeptide and administering a polynucleotide does not

necessarily reveal art on each other, and is therefore burdensome. Further, although all claims depend from claim 1, the claims are still drawn to different products and methods. Therefore the restriction requirement is deemed proper and made FINAL.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 20, line 8. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite an HCV Core polypeptide or fragment thereof. It is not clear what "fragment" is being referred to. In its broadest interpretation the fragment could be a single amino acid. Suggested language is "immunologically active fragment". Clarification is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Bartenschlager *et al.* (*Journal of Virology* (1993) 67:3835-3844). The claims are drawn to an isolated mutant non-structural HCV polypeptide comprising a polypeptide having a mutation in the catalytic domain of NS3, wherein said mutation functionally disrupts the catalytic domain. The mutation can be a deletion or substitution. According to Applicant's specification, the catalytic domain of NS3 is defined as the protease active site region, see page 11, lines 19-20. The Bartenschlager reference discloses isolated mutant HCV NS3 polypeptides having substitutions and deletions rendering the protease non-functional (functionally disrupting the catalytic domain), see abstract. Therefore claims 1-3 are anticipated by the Bartenschlager reference.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-19 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bartenschlager *et al.* (*Journal of Virology* (1993) 67:3835-3844) in view of Houghton *et al.* (EP

0693687) and Miyamura *et al.* (U.S. Patent 5,372,928). The claims are drawn to an isolated mutant non-structural HCV polypeptide comprising a polypeptide having a mutation in the catalytic domain of NS3, wherein said mutation functionally disrupts the catalytic domain. The mutation can be a deletion or substitution, and the polypeptide can also contain NS4a, NS4b, NS5a, NS5b, C (core), E (envelope), SEQ ID NO: 9, and various combinations thereof. Also claimed is a pharmaceutical composition comprising the mutant NS3 polypeptide and a pharmaceutically acceptable excipient.

The Bartenschlager reference discloses isolated mutant HCV NS3 polypeptides having substitutions and deletions rendering the protease non-functional (functionally disrupting the catalytic domain), see abstract. Bartenschlager does not suggest different combinations of the mutant NS3, NS4a, NS4b, NS5a, NS5b, C (core), E (envelope) and SEQ ID NO: 9, nor does Bartenschlager suggest the proteins as pharmaceutical components, rather they are disclosed as diagnostics.

However, Houghton *et al.* disclose combinations of HCV antigens for use in immunoassays to detect anti-HCV antibodies. The combinations comprise truncated NS3 (preferably having at least amino acids 1192-1457 of NS3 immunodominant epitope), C, S, NS3, NS4, NS5 and SEQ ID NO: 9, see claims 1-14, figure 1 and page 4, lines 25-27. Houghton teaches that the C nucleocapsid domain extends from the N-terminal to approximately amino acid 120, see page 4, lines 3-7, and that it is preferred that the C domain antigen comprise a majority of the entire sequence of the domain (which ends at amino acid 120), see page 4, lines 19-20.

Miyamura *et al.* discuss multivalent vaccines against HCV comprising E, NS1, C, NS2, NS3, NS4 and NS5 with an appropriate pharmaceutical excipient, see column 18, lines 43-69.

It would have been obvious to substitute the mutant NS3 into the protein compositions taught by Bartenschlager and Miyamura. One would have been motivated by Bartenschlager's discussion disclosing that the serine proteinase of HCV (NS3) may represent a novel target for antiviral drug development, see page 3843, second column, last paragraph. The various combinations of HCV proteins would have been obvious because E, C, NS3, NS4 and NS5 are well known in immunogenic compositions as evidenced by Houghton and Miyamura. One would have had a reasonable expectation of success that the mutant NS3 would work as a diagnostic and immunogen in the compositions of Houghton and Miyamura because Houghton and Miyamura disclose the use of NS3 (truncated in Houghton) in diagnostics and pharmaceuticals. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

It is noted that the novelty of the invention is the mutation of the catalytic domain of NS3 rendering it nonfunctional. In view of the prior art, the novelty of the invention is either anticipated or obvious. Applicant is invited to clarify how the mutation instantly claimed is a contribution over the mutation described in the Bartenschlager reference.

Conclusion

7. No claim is allowed.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number

for Art Unit 1648 is (703) 308-4426. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy S. Brown, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday and alternate Wednesdays from 6:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stacy S. Brown
February 22, 2002

HANKYEL T. PARK, PH.D
PRIMARY EXAMINER